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EXCEEDING THE DIAMETER: WHEN TO EXAMINE THE AORTA IN CHILDREN WITH CONGENITAL AORTOPATHIES?

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REZUMAT

DEPĂȘIREA DIAMETRULUI AORTEI: CÂND SĂ CERCETĂM AORTA LA COPIII CU AORTOPATII CONGENITALE?

Introducere: Importanța diagnosticului timpuriu al unei complicații din cadrul aortopatiilor congenitale/ (genetice AoC/G) la copii a fost demonstrată de rezultatele studiului nostru.

Scopul lucrării: Aprecierea scorului Z al diametrelor la diferite segmete ale aortei toracice.

Material și metode: Studiu analitic, observațional, de cohortă. Au fost admiși 150 de copii. Programul statistic utilizat - SPSS versiunea 20.

Rezultate: În rezultatul cercetării copiilor cu aortopatii congenitale/genetice s-a confirmat prezența dilatării aortice (scorul Z>2DS) **în coarctație de aortă:** la nivelul diametrului inelului valvular (22,9%), sinusului Valsalva (25,0%), joncțiunii sino-tubulare (8,3%) și a arcului aortic (20,8%); în **stenoza aortei și valva aortică bicuspidă:** la nivelul diametrului aortei ascendente (36,8%) și descendente (31,6%); în **sindroamele genetice:** la nivelul diametrului inelului valvular (33,3%) și al aortei ascendente (50,0%); analiza coeficientul de corelație între cele 6 diametre certifică ipoteza conform căreia o dilatare la cel puțin un segment aortic devine un factor de risc pentru dezvoltarea acesteia și la celelalte nivele ale arcului aortic.

Concluzii: Rezultatele studiului au indicat că morfometria aortei și calcularea scorului Z ale diametrelor aortice sunt utile și practice în prevenirea unei complicații din AoC/G la copii.

Cuvinte-cheie: aortopatii congenitale / genetice, copii, complicații.

РЕЗЮМЕ

ПРЕВЫШЕНИЕ ДИАМЕТРА АОРТЫ: КОГДА ОБСЛЕДОВАТЬ АОРТУ У ДЕТЕЙ С ВРОЖДЕННЫМИ АОРТОПАТИЯМИ?

Введение: Важность ранней диагностики осложнения врожденных аортопатий ВАо у детей была продемонстрирована результатами нашего исследования.

Цель работы: оценка Z-диаметров в разных сегментах грудной аорты.

Материал и методы: аналитическое, наблюдательное, когортное исследование. 150 детей были обследованы. Используемая статистическая программа - версия 20 SPSS.

Результаты: В результате исследования детей с врожденной / генетической аортопатией было подтверждено наличие дилатации аорты (Z балл > 2SD) при коарктации аорты: на уровне диаметра кольца клапана (22,9%), синусового узла Вальсальвы (25,0%), синус-соединения трубчатая (8,3%) и дуга аорты (20,8%); при стенозе аорты и двустворчатом аортальном клапане: на уровне восходящего (36,8%) и нисходящего (31,6%) диаметра аорты; при генетических синдромах: на уровне диаметра клапанного кольца (33,3%) и восходящей аорты (50,0%); Анализ коэффициента корреляции между шестью диаметрами подтверждает гипотезу, согласно которой расширение по меньшей мере одного сегмента аорты становится фактором риска его развития на других уровнях дуги аорты.

Выводы. Результаты исследования показали, что морфометрия аорты и Z-оценка диаметра аорты полезны и практичны в предотвращении осложнений ВАо у детей.

Ключевые слова: врожденные / генетические аортопатии, дети, осложнения.

INTRODUCTION

Congenital aortopathies (CAo) lead to increased global cardiovascular mortality, both in childhood and in adulthood. These entities include: aortic stenosis (AoS), aortic coarctation (AoC), bicuspid aortic valve (BAV), but also genetic diseases involving the aorta: Marfan syndrome (MS), Ehlers-Danlos syndrome, Turner syndrome, and others (1,2). According to the estimated incidence in the specialty literature, aortic stenosis constitutes 2-11% of the total number of congenital heart diseases (CHD) in children, with a prevalence of 3-5 cases per 1000 live births. Aortic coarctation (AoC) accounts for 5-8% of cases, with a prevalence of 3 to 10.000 live births. Aortic dilatation occurs in 0.4% of patients with CAo, aortic valvulopathies (BAV) are the most common malformations (prevalence 1-2%) and have a risk of dissection up to 40% (2,3). In children, as opposed to adults, aortopathies are sometimes completely asymptomatic, which camouflages the suspicion of developing a complication. Congenital aortopathies require early diagnosis and prompt therapy to improve the extremely unfavorable prognosis in some cases.These patients have the clinical symptoms of cardiac or vascular remodeling installed over time.In this context, the assessment of aortic dilation and the type of aortic dilation is essential for predicting the possible complication in development at children with CAo.

Based on these assumptions and beliefs, we would like to emphasize the value of this research project in order to determine the prognostic elements capable of positively influencing the future of children with CAo.

MATERIAL AND METHODS

To achieve *the purpose and objectives of the research,* an analytical follow-up study was planned.

*General design and study population.*During 2016–2019, 150 children with CAo were examined complex, according to the study protocol developed. The study project was carried out within the IMPH IMC, at theDepartment of Pediatrics of the Pediatric Cardiology Clinic. At the initial stage, the 150 selected children with CAo were subjected to a complex examination, by investigation, after a clinical-paraclinical examination, and based on the obtained data (two-dimensional echocardiography) and the anthropometric parameters, the Z scores were calculated (Detroit Data) for each diameter of the aorta, criterion that allowed us to appreciate the children with changes in diameter (dilation) at the level of the aorta (score Z>2 DS) (4).

Inclusion criteria were: children aged 1 month to 17 years, 11 months and 29 days with CAo (implicit criterion); diagnosis confirmed by AoS with PG>30 mmHg, CAo operated/unoperated; patients with BAV and genetic syndromes that involve the aorta: Marfan, Turner, etc .; the presence of the agreement to participate in the study by the tutor and the assent from the children ≥14 years old.

Exclusion criteria: children (parents or carers) who refuse to participate in the study; patients with severe concomitant pathologies (renal, hepatic impairment, terminal stage, with severe neurological pathologies); children with acquired (rheumatic) valvulopathies.

The evaluation of patients was performed in the following way:

Stage 1. Using the inclusion and exclusion criteria, 150 children with CAo were admitted to the research, who formed the general research sample, they were subjected to a thorough investigation, specifying the prenatal and postnatal history, disease history, current status. disease; objective physical examination (anthropometric indices: weight, height, body surface area), laboratory examinations of an obstructive type CHD, basic instrumental examinations (two-dimensional EcoCG and color Doppler.)

Stage 2. By means of the two-dimensional echocardiographic examination and the calculation of the Z score, the batch of children with modifications of the aortic diameters was obtained for dilation. Initially the echocardiographic examination based on the morphology of the aorta was performed at 6 levels of the aortic segments: root of the aorta (diameter of the valvular ring, diameter of the sinus Valsalva, diameter of the sinotubular junction); ascending aorta; aortic arch (between the brachiocephalic trunk and left subclavian artery); descending aorta (immediately below the aortic isthmus). Morphometry of the aorta was performed according to Petterson's criteria with the Toshiba Aplio 300 echocardiographic model, type MODUS TUS-A300, and the Z-score calculation - after *Detroit Data* (4). The diameter of the aortic ring was fixed at the distance between the points of articulation of the valves, during systole, in the long axis parasternal ultrasound dial. The diameter of the sinus Valsalva was assessed in the left parasternal section in the maximal size of the systole. Also in the same quadrant, the diameters of the sinotubular junction and the proximal ascending aorta were also appreciated. The diameter of the aortic arch was measured in the suprasternal echocardiographic quadrant, long axis, in the maximum systolic dimension between the brachiocephalic trunk and the left common carotid artery. And the diameter of the proximal descending aorta was measured in the suprasternal quadrant, long axis, in the maximal size of the systole in the immediate vicinity of the aortic isthmus, distal to the left subclavian artery.

Stage 3. Subsequently, the values of the Z score were calculated, online, by introducing the values of the aortic diameter (cm) relative to the area of the child's body surface (height - cm, weight - kg), based on which the study sample appreciated children with diameter changes in the aorta (Z score>2 DS) and children without diameter changes in the aorta (Z score≤2 DS). The first batch consisted of 89 children - 62 boys and 27 girls, with an average age of 102.8 ± 7.13 months, and the second batch - of 91 children (30 ineligible children with Z =2 DS score), respectively 61 children - 48 boys and 13 girls, with an average age of 121.4 ± 7.2 months.

Stage 4. The types of CAo found in the research were investigated, the types of aortic dilatations being evaluated as the risk factors in the development of a complication of the CAo such as aneurysm, dissection, aortic rupture.

Ethical considerations. The consent of the parents or the legitimate guardian and the consent of the children aged ≥14 years were obtained; they were not paid, they did not bear financial expenses related to the study participation. The study was approved by the Research Ethics Committee of the State University of Medicine and Pharmacy NicolaeTestemitanu (report No. 76 of 12.05.2017).

The given scientific research is an analytical tracking study, in which several statistical methods were used: historical, comparative, biostatistic, observational, mathematical.

*Statistical analysis.*The statistical analysis of the obtained results was performed by several methods of assessing the truthfulness: the $\chi 2$ matching criterion, the U-Fisher criterion, the t-Student criterion of comparing the mean values, the correlation analysis, the Odds Ratio (OR), the discriminant analysis, the analysis logistic regression.

RESULTS

Despite the multiple researches that had as objective the evaluation and definition of the evolutionary particularities of the CAo, there are still many obscure and contradictory moments regarding the interpretation of the character of the structural changes in dynamics in the context of the clinical manifestations in children with these pathologies. The essence of the correct and timely approach of a child with CAo is to evaluate the risk of developing a complication (dilatation, aneurysm, dissection) with the potential for premature death, and one of the main components of this approach is the long-term follow-up, with the appreciation of the elements displayed by expansion to certain levels of the aorta.

Analysis of the distribution of the study participants according to age groups. The study included children aged 1 month to 17 years 11 months and 29 days (mean age =10 ± 5.19 months or 9.2 years). These children were divided into two groups according to the aortic diameter changes presented. One batch of children were those with larger (expanded) diameters and another batch the children with unchanged diameters. Group I consisted of 89 children (59.3%), of whom 18 (20.2%) aged≤1 year (≤12 months), 11 (12.4%) aged 1– 5 years (12–60 months), 29 (32.6%) aged 5-12 years (60–144 months) and 31 (34.8%) aged >12 years. Group II consisted of 61 (40.6%) children, of which one (1.6%) under the age of ≤ 1 year (≤12 months), 10 (16.4%) aged between 1 and 5 years (12–60 months), 26 (42.6%) 5–12 years (60–144 months) and 24 (39.6%) over 12 years.

According to the data presented in Table 1, there is a presence of CAo with changes in diameter at the level of the aorta (score Z>2DS) in subjects aged ≤1 year (≤12 months) in 20.2% cases, confirming the possibility of installation of the expansive type complications (dilation, dissection, aortic rupture) from an early age.

Analysis of the distribution of study participants according to the environment of origin. The prevalence of children from rural versus urban areas was recorded in the study, the same legality being maintained in the research groups, respectively 74 (83.1%) of children from group I and 51 (83.6%) from group II were from the rural area vs 15 (16.9%) and 10 (16.4%) children of urban origin ($\chi 2$ = 0.006; p>0.05).

The structure of the subjects included in the research according to the type of congenital / genetic aortopathy. The general group of children included the following groups of aorta pathologies: the first group was represented by children with AoS – 38.0%, the second group was made up of children with AoC – 32.0%, the third group was formed of children with BAV – 26.0%, and the fourth group included children with the genetic syndromes – 4.0%, a separate group constituted the combined pathologies: AoS + BAV – 29.0% of the total subjects and, AoS + AoC – 17.03%, (Figure 1).

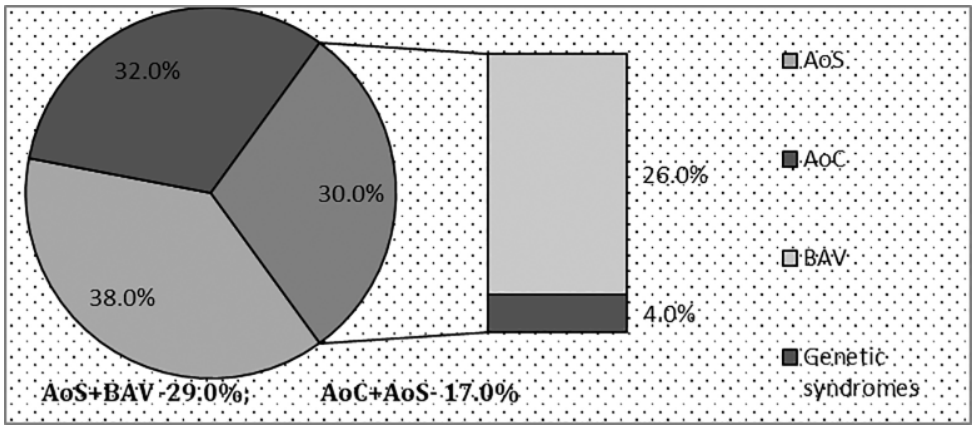

Figure 1. Structure of the subjects included in the research according to the type of congenital and genetic aortopathy and their combinations

Note: AoC-Aortic coarctation, AoS-Aortic stenosis, BAV-bicuspid aortic valve

*Aortic diameters and Z score.*The diameters were estimated at six segments of Ao, being related to the area of the body surface.Z-score assessment - a method of highlighting the deviation of the value of a certain parameter evaluated from the average population specific to size or age, used in both cardiology and pediatric echocardiography- was performed in subjects with or without changes in diameter in the aorta.An increased Z-score was considered informative for the suspicion and detection of progressive dilation of aortic diameters in a child with CAo, warning the clinician of the risk of developing a complication even during harmonious physical development.

*Aortic diameters of CAo children in group I through the Z score.*In the research, the evaluation of the aortic diameters (Ø) was performed based on the Z score, obtaining the following results:

Z score of Ao valve ring Ø. The value of the score Z <2 SD was recorded at 61 (68.5%), and ≥2 SD – at 28 (31.5%) participants ($\chi2 = 23.5$; $p = 0$).

Z score of the Valsalva sinus Ø. The value of the Z <2 SD score was attested in 66 (74.2%), and ≥2 SD – in 23 (25.8%) children ($\chi2 = 18.6$; $p = 0$).

Z score of sinotubular junction Ø. The value of the Z <2 SD score was present in 82 (92.1%), and ≥2 SD - in 7 (7.9%) subjects ($\chi2 = 5.03$; $p < 0.05$).

Z score of ascending Ao Ø. The value of the score Z <2 SD was recorded at 44 (49.4%), and ≥2 DS - at 45 (50.6%) participants ($\chi2 = 44.06$; $p = 0$).

Z score of aortic arch Ø. The value of the Z <2 SD score was present in 76 (85.4%), and ≥2 SD – in 13 (14.6%) subjects ($\chi2 = 9.7$; $p < 0.01$).

Z score of descending Ao Ø. The value of the Z <2 SD score was noted in 51 (57.3%), and ≥2 SD – in 38 (42.7%) children ($\chi2 = 34.8$; $p = 0$). The respective data are presented in Figure 2.

When evaluating the six aortic diameters according to the type of CAo the following results were obtained:

- The diameter of the aortic valve ring (I) had values of the Z score ≥2 SD in AoS - in 7 (12.3%) cases, in AoC - 11 (22.9%), in BAV - 8 (20.5 %), in genetic syndromes - 2 (33.3%), p>0.05.
- Valsalva (II) sinus diameter recorded values of Z score ≥2 SD in AoS - in 6 (10.5%) cases, in AoC - 12 (25%), in BAV - 4 (10.3%), in genetic syndromes - 1 (16.7%) case (p>0.05).
- The diameter of the sinotubular junction (III) showed values of the Z score ≥2 SD in AoS - 1 (1.8%) case, in AoC - 4 (8.3%), in BAV - 2 (5.1%), in genetic syndromes - 0 cases (p>0.05).
- The diameter of the ascending aorta (IV) had values of the Z score ≥2 SD within AoS - in 21 (36.8%) cases, in AoC - 10 (20.8%), in BAV - 11 (28.2%), in genetic syndromes - 3 (50.0%) cases (p>0.05)
- The diameter of the aortic arch (V) showed values of the score Z ≥2 SD in AoS - 2 (3.5%), in AoC - 10 (20.8%), in BAV - 1 (2.6%), in genetic syndromes - 0 cases (p>0.01).
- The diameter of the descending aorta (VI) recorded values of the Z score ≥2 SD in AoS - recorded 18 (31.6%) cases, in AoC - 11 (22.9%), in BAV - 8 (20.5%), in genetic syndromes - 1 (16.7%) case (p>0.05), table 1.

The results obtained are similar to those in the literature, according to which the classic paraclinical data of an CAo can be quite variable and can present a risk of dissection, without a priori aortic dilation.

Existing studies demonstrate an increased rate of complications in subjects with CAo, especially in combination cases (AoC + BAV). Aortic dilatation can occur in different aortic segments, appearing in a bulbar form that is installed at the root of the aorta, and the tubular type - at the level of the ascending aorta. Knowing the type of dilation and the level of impairment in a given CAo facilitates the prediction of aneurysm, dissection or aortic rupture. Two pathologies are known to present an increased risk of aortic dissection, these being the aortic

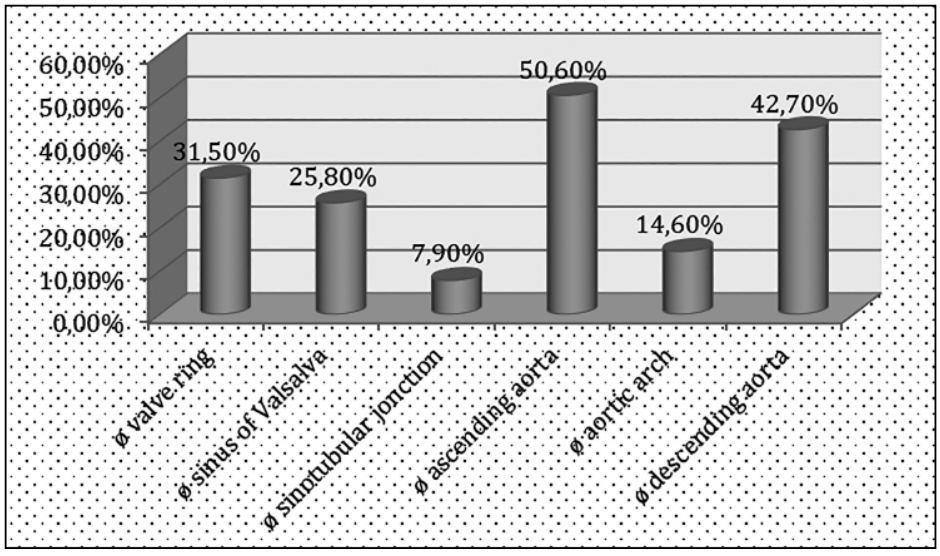

Figure 2. Aortic diameter values > 2 SD of the Z score in CAo children in the research group

Table 1.

Z score of aortic diameters by congenital aorthopaties type in children

Z score	Total		Congenital aorthopaties							
	N	%	AoS		AoC		BAV		Genetic sdr.	
			N	%	N	%	N	%	N	%
The diameter of the aortic valve ring (I) – χ^2=3,04; p>0,05										
=2 SD	122	81,3	50	87,7	37	77,1	31	79,5	4	66,7
>2 SD	28	18,7	7	12,3	11	22,9	8	20,5	2	33,3
Total	150	100,0	57	100,0	48	100,0	39	100,0	6	100,0
Valsalva sinus diameter (II) – χ^2=5,25; p>0,05										
=2 SD	127	84,7	51	89,5	36	75,0	35	89,7	5	83,3
>2 SD	23	15,3	6	10,5	12	25,0	4	10,3	1	16,7
Total	150	100,0	57	100,0	48	100,0	39	100,0	6	100,0
The diameter of the sinotubular junction (III) – χ^2=2,85; p>0,05										
=2 SD	143	95,3	56	98,2	44	91,7	37	94,9	6	100,0
>2 SD	7	4,7	1	1,8	4	8,3	2	5,1		
Total	150	100,0	57	100,0	48	100,0	39	100,0	6	100,0
The diameter of the ascending aorta (IV) – χ^2=4,39; p>0,05										
=2 SD	105	70,0	36	63,2	38	79,2	28	71,8	3	50,0
>2 SD	45	30,0	21	36,8	10	20,8	11	28,2	3	50,0
Total	150	100,0	57	100,0	48	100,0	39	100,0	6	100,0
The diameter of the aortic arch (V) – χ^2=13,2; p>0,01										
=2 SD	137	91,3	55	96,5	38	79,2	38	97,4	6	100,0
>2 SD	13	8,7	2	3,5	10	20,8	1	2,6		
Total	150	100,0	57	100,0	48	100,0	39	100,0	6	100,0
The diameter of the descending aorta (VI) – χ^2=2,04; p>0,05										
=2 SD	112	74,7	39	68,4	37	77,1	31	79,5	5	83,3
>2 SD	38	25,3	18	31,6	11	22,9	8	20,5	1	16,7
Total	150	100,0	57	100,0	48	100,0	39	100,0	6	100,0

bicuspid (risk of dissection estimated at 0.4%) and Marfan syndrome (≈ 40% of the subjects develop acute acute aortic dissection.

type of this dilation as a risk factor in the occurrence of a complication of giant aneurysm type and/or aortic dissection. The results obtained are shown in Figure 3.

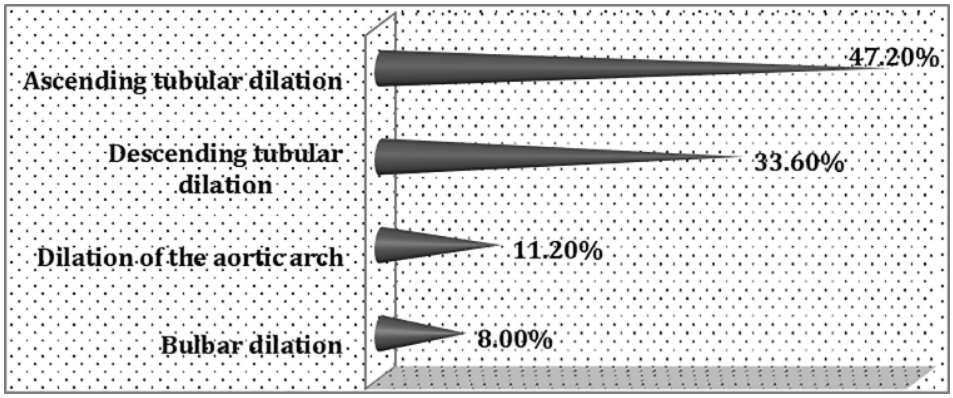

Figure 2. Types of dilatations in children with congenital aortopathies

Analysis of the types of dilatations at the level of the aorta as risk factors in the specific complications of congenital aortopathies in children. Having confirmed the types of CAo in children and performing at the initial stage the distribution of the general group according to the presence or absence of aortic dilation in relation to anthropometric indices (Z score), we considered it essential to assess the

In the research conducted, evaluating the dilated aortic diameters, we found that on the first place is the dilation of the ascending aorta, which usually has a tubular dilation - 42 (47.2%) of children. In the second place is the dilation of the descending aorta - the isthmus, recorded in 29 (33.6%) participants in the study. Subsequently, 10 (11.2%) cases showed dilatation in the diameters of the

aortic valve ring and the transverse aortic arch, and in the Valsalva sinus - bulbar dilation in only 7 (8.0%) children. The association of dilated segments of the aorta is commonly found in CAo. In about 7.9% (n=7) of cases, the children showed dilatation of diameters at the level of two different aortic portions: the segment of the ascending aorta with the segment of the descending aorta and the level of the aortic valvular ring with the portion of the sinus Valsalva. In 4.5% (n=4) cases they developed aortic diameter dilatation concomitantly at the level of the aortic valve ring and in the isthmus portion of the descending aorta; the rest of the combinations were recorded in unique cases.

The specificity of the development of the complications within the congenital aortopathies is depending on the type of aortic dilatation which in turn depends on the type of congenital aortopathy confirmed. Thus, studies have shown that: ascending tubular dilation is with tropism over the bicuspid aortic valve, aortic stenosis and both are most commonly complicated by aortic dissection (5). Bulbar dilation is a greater risk of developing an aortic rupture dissection and we may have it at a higher rate in the genetic syndromes with aortic defect (Marfan syndrome) (6). Within aortic coarctations and genetic syndromes, such as Turner syndrome, the descending tubular dilatation is associated with the risk of aortic aneurysms (7).

DISCUSSIONS

The research papers reported in recent years pay close attention to the factors that may favor the development of major complications in CHD (8). In this context, a particular role is played by a category of valvulo-vascular CHD of obstructive type, with major risk of developing lethal complications, because they arise with an expansive mechanism post-obstruction (1,5). This group of cardiac malformations are congenital aortopathies (CAo) - relatively new concept in pediatric cardiology of the Republic of Moldova. Given the increased incidence of CAo (about 10-15%) in the total CHD in children, we initiated this research in a group of children (1,6).

Congenital aortopathies lead to increased global cardiovascular mortality, both in childhood and in adulthood. In children, as opposed to adults, aortopathies are sometimes completely asymptomatic, which camouflages the suspicion of developing a complication (9). Congenital aortopathies require early diagnosis and prompt therapy to improve the extremely unfavorable prognosis in some cases. Recently, the Global Burden Disease Project 2010 demonstrated that the overall mortality rate from CAo complications (aneurysms, dissections, aortic rupture) increased from 2.49 to 100.000 inhabitants to 2.78 to 100.000 in the years 1990-2010, with higher rates for males (2,10). The information presented demonstrates the topicality of the topic and the importance of its research. The treated subject is fundamental and extremely interesting regarding the consequences that we can monitor by studying the evolution of a certain type of congenital aortopathy. And researching the factors involved in the occurrence of a complication, so the type of aortic dilation can prevent a complication can sometimes be fatal. These factors have a predictive role in the prophylaxis of valvulo-vascular remodeling, developed progressively in children with CAo (11).

The discriminant selective analysis of the study group allowed to highlight groups of risk factors for the probability of occurrence of a specific CAo complication: factors related to the type of CAo and factors related to the type of aortic dilation.

CONCLUSIONS

1. The type of CAo, according to the obtained results, plays an important role in the appearance of dilation, aneurysm, dissection, aortic rupture, in the study being recorded not only CAo as isolated entities (AoS, AoC, BAV, genetic syndromes), but also valvulo- vascular combinations (BAV + AoS, BAV + AoC, BAV + genetic syndromes etc.)
2. As a result of the research of children with congenital aorthopaties, the presence of aortic dilation was confirmed (Z score>2 SD), in **aortic coarctation**: at the level of the diameter of the valve ring (22.9%), of the Valsalva sinus (25.0%), of the sino-tubular jonction (8.3%) and aortic arch (20.8%); **in aortic stenosis and bicuspid aortic valve**: at the diameter of the ascending (36.8%) and descending aorta (31.6%); **in genetic syndromes**: at the diameter of the valve ring (33.3%) and the ascending aorta (50.0%). The analysis of the correlation coefficient between the 6 diameters certifies the hypothesis according to which a dilation at at least one aortic segment becomes a risk factor for its development at the other levels of the aortic arch.
3. The analysis of the types of dilations at the level of Ao as risk factors in the complications of CAo in children found that the dilatation of the ascending aorta is on the first place, which usually has a tubular dilation (47.2%); on the second place is the dilation of the descending aorta, the isthmus portion (33.6%). In 10 (11.2%) cases, there were dilations in the diameters of the aortic valve ring (11.2%), the transverse aortic arch (11.2%) and the Valsalva sinus (8.0%).

CONFLICT OF INTERESTS

The authors do not declare any conflict of interest.

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